Amendments to the Specification:

Please replace the paragraph beginning at page 1, line 7 with the following re-written paragraph:

A1

This application is a continuation-in-part of application Ser. No.09/738,879 filed on December 18, 2000~~.~~, claiming priority of the Italian application No. MI2000A000665 filed on 30 March 2000.

Please replace the paragraph beginning at page 10, line 19 with the following re-written paragraph:

A2

The solution containing the epimerized product of step c) at a concentration of 10% is cooled at 10°C and passed through an IR 120 H^+ column or equivalent (35-100 ml). Both the column and the container of the product are kept at 10°C. After the passage of the solution the resin is washed with deionized water until the pH of the flow through is more than 6 (about 3 volumes of deionized water). The acidic solution is kept to neutrality with a tertiary or quaternary amine such as tetrabutylammonium ~~tetrabuthylammonium~~ hydroxide (15% aqueous solution) obtaining the ammonium salt of the polysaccharide. The solution is concentrated to the minimum volume and freeze dried. The product obtained is suspended in 20-500 ml of dimethyl formamide (DMF) or dimethyl sulfoxide (DMSO) and added with 15-300 g of a sulfating agent such as the adduct pyridine .SO_3 in the solid form or in solution of DMF or DMSO. The solution is kept at 20-70°C, preferably between 40 and 60°C for 2-24 hours.

Please replace the paragraph beginning at page 11, line 25 with the following re-written paragraph:

A3

The solution containing the product of step (e) is treated as described in step (d) to obtain the tertiary amine or quaternary ammonium salt, but performing the reaction at 20-25°C. The

ammonium salt is suspended in 20-500 ml of DMF. The suspension is cooled to 0°C and treated with an amount of sulfating agent such as the adduct pyridine.SO_3 calculated in function of the percentage of the sulfate in position 6 of the amino sugar to be inserted taking in account a minimum of 60% of 6-O sulfation calculated as described above. The quantity of sulfating agent is comprised between two and ten equivalents of the hydroxyl groups to be sulfated. The sulfating agent is added one step or with several additions in a total time of 20 minutes.

A3 concld

Please replace the paragraph beginning at page 15, line 12 with the following re-written paragraph:

Thus, it is a further object of the present invention to provide a process for the preparation of novel glycosaminoglycans, which comprises

(i) reacting K5 with a N-deacetylating agent, then treating the N-deacetylated product with a N-sulfating agent;

(ii) submitting the N-sulfate K5 thus obtained to a C5-epimerization by glucuronosyl C5 epimerase to obtain a C5-epimerized N-sulfate K5 in which the iduronic/glucuronic ratio is from 60/40 to 40/60;

A4

(iii) converting the C5-epimerized N-sulfate K5, having a content of 40 to 60% iduronic acid over the total uronic acids, into a tertiary amine or quaternary ammonium salt thereof, then treating the salt thus obtained with an O-sulfating agent in an aprotic polar solvent at a temperature of 40-60°C for 10-20 hours;

(iv) treating an organic base salt ~~a salt with an organic base~~ of the O-oversulfated product thus obtained with a mixture dimethyl sulfoxide/methanol at 50-70 °C for 135-165 minutes;

(v) treating an organic base salt ~~a salt with an organic base~~ of the partially O-desulfated product thus obtained with an O-sulfating agent at a temperature of 0-5°C;

(vi) treating the product thus obtained with a N-sulfating agent;

whatever product obtained at the end of one of steps (ii) to (vi) being optionally submitted to a depolymerization.

Please replace the paragraph beginning at page 16, line 24 with the following re-written

paragraph:

Step (iii), consisting of an O-oversulfation, is carried out by previously converting the C5 epimerized N-sulfate K5 into a tertiary amine or quaternary ammonium salt thereof and then by treating said salt with an O-sulfating agent at a temperature of 40-60°C for 10-20 hours. Typically, the solution containing the epimerized product of step (ii) at a concentration of 10% is treated as illustrated above for step (d) of oversulfation, in particular by heating a solution of the above salt in DMF or DMSO at 20-70°C for 2-24 hours, preferably at 40 - 60°C for 15-20 hours.

Please replace the paragraph beginning at page 17, line 29 with the following re-written paragraph:

Step (v), consisting of a 6-O-sulfation, must also be carried out if, after a depolymerization step following step (vi) below, compounds having a high antithrombin activity, anti-Xa, HCII activities as high as those of heparin and a low aPTT are desired. The selective 6-O-sulfation is carried out by converting the selectively O-desulfated product into a tertiary amine or quaternary ammonium salt thereof and treating said salt with an O-sulfating agent at low temperature, more particularly at 0-5°C for 0.5-3 hours. Typically, the 6-O-sulfation is carried out as illustrated above for step (f) of O-sulfation. The solid obtained is purified by diafiltration as described in step (iv). A small amount is freeze dried for the structural analysis by ^{13}C-NMR. If the content of 6-O sulfate groups calculated by NMR, as described by Casu et al. Arzneimittel-Forschung Drug Research, 1983, 33, 135-142.

Please replace the paragraph beginning at page 19, line 9 with the following re-written paragraph:

The novel C5 epimerized N,O-sulfate K5 glycosaminoglycans obtained at the end of the process of the present invention are generally isolated in form of their sodium salt. Said sodium salt may be converted into another salt. Said other salt may be another alkaline metal salt or an alkaline-earth metal, ammonium, tetra (C_1-C_4)alkylammonium, ~~(C_1-C_4) trialkylammonoim~~ aluminium or zinc salt.

tetra (C_1-C_4)alkylammonium

A7 cont'd

Advantageously, said other salt is another alkaline metal, an alkaline-earth metal, ammonium, tetra (C_1-C_4)alkylammonium, aluminium or zinc salt.

Please replace the paragraph beginning at page 19, line 22, continuing to page 20, line 6 with the following re-written paragraph:

Thus it is a further object of the present invention to provide novel C5-epimerized N,O-sulfate K5 glycosaminoglycans obtainable by a process which comprises

(i) reacting K5 with a N-deacetylating agent, then treating the N-deacetylated product with a N-sulfating agent;

(ii) submitting the N-sulfate K5 thus obtained to a C5-epimerization by glucuronosyl C5 epimerase to obtain a C5-epimerized N-sulfate K5 in which the iduronic/glucuronic ratio is from 60/40 to 40/60;

A8

(iii) converting the C5 epimerized N-sulfate K5, having a content of 40 to 60% iduronic acid over the total uronic acids, into a tertiary amine or quaternary ammonium salt thereof, then treating the salt thus obtained with an O-sulfating agent in an aprotic polar solvent at a temperature of 40-60°C for 10-20 hours;

(iv) treating an organic base salt ~~a salt with an organic base~~ of the O-oversulfated product thus obtained with a mixture dimethyl sulfoxide/methanol at 50-70 °C for 135-165 minutes;

(v) treating an organic base salt ~~a salt with an organic base~~ of the partially O-desulfated product thus obtained with an O-sulfating agent at a temperature of 0-5°C;

(vi) treating the product thus obtained with a N-sulfating agent;

whatever product obtained at the end of one of steps (ii) to (vi) being optionally submitted to a depolymerization and the sodium salt of the end product being optionally converted into another salt.

Please replace the paragraph beginning at page 21, line 14 with the following re-written paragraph:

A9

In this context, the expression "chemically acceptable" is referred to a cation which is

A9 cont'd

useful for the chemical syntheses, such as ammonium or ~~(C1-C4)trialkylammonium~~ tetra(C_1-C_4)alkylammonium ion, or for the purification of the products.

Please replace the paragraph beginning at page 21, line 28 with the following re-written paragraph:

A10

Preferred glycosaminoglycans of this class is constituted by a mixture of chains with a mean molecular weight of from about 6,000 to about 8,000, in which at least 90% of said chains have the formula I above, wherein about 55% of the uronic acid units are those of iduronic acid and R_3 is from about 85% to about 90% SO_3^-; R_2 is about 20% SO_3^-; R_1 is from about 25% to about 30% SO_3^- in iduronic units and 0 to about 5% SO_3^- in glucuronic units; R is from about 30% to about 35% SO_3^- in glucuronic units and 0 to about 5% in iduronic units; the sum of SO_3^- percent in R_1, glucuronic units, and in R, iduronic units, is about 5%; R_1 and R being not simultaneously SO_3^- and being both hydrogen in from about 30% to about 40% of the uronic acid units; the sulfation degree being from about 2.5 to about 2.7, the corresponding cation being a chemically or pharmaceutically acceptable one.

Please replace the paragraph beginning at page 22, line 22 with the following re-written paragraph:

A11

Advantageous chemically and pharmaceutically acceptable cations are those derived from alkaline metals, alkaline-earth metals, ammonium, tetra (C_1-C_4) alkylammonium, ~~(C_1-C_4)trialkylammonium~~ aluminium and zinc, sodium and calcium ions being particularly preferred.